

**WHAT IS CLAIMED IS:**

1. A transgenic mouse whose somatic and germ cells comprise a disruption in an endogenous histamine H3 receptor, wherein said disruption is generated by targeted replacement with a non-functional histamine H3 receptor, and wherein said disruption results in said mouse having an insensitivity to amnesic effects of scopolamine as compared to wild-type histamine H3 receptor mice.
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2. The mouse of claim 1, wherein said mouse is fertile and transmits the non-functional histamine H3 receptor gene to its offspring.  
10 *LAB*
3. The mouse of claim 1, wherein the non-functional histamine H3 receptor gene has been introduced into an ancestor of the mouse at an embryonic stage by microinjection of embryonic stem cells into mouse blastocysts.
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4. The mouse of claim 1, wherein the non-functional histamine H3 receptor gene has been introduced at an embryonic stage by microinjection of embryonic stem cells into a mouse blastocyst.
- 20 5. A method for producing a transgenic mouse whose somatic and germ cells comprise a disruption in an endogenous histamine H3 receptor gene, wherein said disruption is generated by targeted replacement with a non-functional histamine H3 receptor gene, said method comprising:
- 25     a) introducing a histamine H3 receptor gene targeting construct comprising a selectable marker into a mouse embryonic stem cell;
- b) introducing the embryonic stem cell into a mouse blastocysts;
- c) transplanting the blastocyst into a recipient pseudopregnant mouse;

- d) allowing the blastocyst to develop to term;
- e) identifying a transgenic mouse whose genome comprises a disruption of the endogenous histamine H3 receptor gene in at least one allele; and
- 5 f) breeding the mouse of step (e) to obtain a transgenic mouse whose genome comprises a homozygous disruption of the endogenous histamine H3 receptor gene, wherein said disruption results in said mouse having an insensitivity to amnesic effects of scopolamine as compared to wild-type histamine H3 receptor mice.

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- 6. The method of claim 5 wherein the introducing of step (a) is by electroporation or microinjection.
  - 15 7. A cell isolated from the transgenic animal of claim 1.

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